

CLAIMS

We claim:

1. A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:
 - (A) receiving a protein backbone structure with variable residue positions;
 - (B) establishing a group of potential rotamers for each of said variable residue positions, wherein at least one variable residue position has rotamers from at least two different amino acid side chains; and,
 - (C) analyzing the interaction of each of said rotamers with all or part of the remainder of said protein structure to generate a set of optimized protein sequences, wherein said analyzing step includes a split singles Dead End Elimination (DEE) with a split flags computation.
2. A method according to claim 1 wherein said analyzing step includes the use of at least one scoring function.
3. A method according to claim 1 wherein said analyzing step includes a Hybrid Exact Rotamer Optimization (HERO) step.
4. A method according to claim 1 wherein said set of optimized protein sequences comprises the globally optimal protein sequence.
5. A method according to claim 1 further comprising testing at least one member of said set to produce experimental results.
6. A method according to claim 4 further comprising:
 - (D) generating a rank ordered list of additional optimal sequences from said global optimal protein sequence.
7. A method according to claim 6 wherein said generating includes the use of a Monte Carlo search.
8. A method according to claim 1 wherein said analyzing step comprises a Monte Carlo computation.
9. An optimized protein sequence generated by the method of claim 1.
10. A nucleic acid sequence encoding a protein sequence according to claim 9.
11. An expression vector comprising the nucleic acid of claim 10.

12. A host cell comprising the nucleic acid of claim 10.

13. A computer readable memory to direct a computer to function in a specified manner, comprising:

a side chain module to correlate a group of potential rotamers for residue positions of a protein backbone model;

a ranking module to analyze the interaction of each of said rotamers with all or part of the remainder of said protein to generate a set of optimized protein sequences wherein said analysis includes a split singles DEE with a split flags computation.

14. A computer readable memory according to claim 13 wherein said ranking module includes a HERO computation step.

15. A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein backbone structure with variable residue positions;

(B) establishing a group of potential rotamers for each of said variable residue positions, wherein the group of potential rotamers for at least one of said variable residue position has a rotamer selected from each of at least two different amino acid side chains; and

(C) analyzing the interaction of each of said rotamers with all or part of the remainder of said protein backbone structure to generate a set of optimized protein sequences, wherein said analyzing step includes a split singles DEE with split flags computation.